REMARKS

I. INTRODUCTION

Claims 51-64 are currently pending in the above-referenced application. By the present amendment, claims 51 and 57 have been amended without prejudice. No new matter has been added herein by the present amendment, as the recitation of the claimed mammal populations have simply been moved in claims 51 and 57 from the preamble to the body of each claim. Applicant respectfully submits that the pending claims are now in condition for allowance.

II. INTERVIEW SUMMARY

Applicant thanks Examiner Patricia Duffy for the courtesy extended during an interview at the USPTO with Michael Levy, Dr. Andrew Bersten and Kevin Godlewski on May 17, 2007. During the interview, the following was discussed:

(A) No exhibit or demonstration was shown.

(B) All claims were discussed, particularly independent claims 51 and 57.

(C) Doyle *et al.* (Advances in Critical Care Testing, Eds. Muller and McQueen, Springer-Verlag Telos, January 1997; reference A17 on the PTOL-1449 of 10/18/00) was discussed.

(D) The possibility of adding further dependent claims to further characterize the claimed method was discussed.

(E) Applicant pointed out the distinction between an "asymptomatic" individual as recited in the claims, and a "normal" individual as disclosed in Doyle *et al.*,

and how a "normal" individual therein is not necessarily an "asymptomatic" individual. Applicant also pointed out that the pending claims, by reciting "said mammal," render the mammal populations recited in the preamble of the independent claims to be claim elements.

(F) It is not believed that other pertinent issues were discussed.

(G) Applicant indicated that a Response to the final Office Action mailed on April 17, 2007 would be submitted summarizing the arguments made during the interview.

(H) There was no e-mail communication.

III. REJECTIONS UNDER 35 U.S.C. § 102(b)

Claims 51-64 stand rejected under 35 U.S.C. § 102(b) as being anticipated by Doyle *et al.* (Advances in Critical Care Testing, Eds. Muller and McQueen, Springer-Verlag Telos, January 1997; reference A17 on the PTOL-1449 of 10/18/00). In discussing the anticipation rejection, the Office Action states that "both [the normal group and the OD group with no evidence of cardiorespiratory disease] necessarily and inherently meet the patient population screened and would be so recognized by the skilled artisan. Although not using the identical language, the patient populations are not distinguished nor is the method." (Office Action mailed on April 17, 2007, page 3). For at least the following reasons, Applicant respectfully submits that Doyle *et al.* does not disclose or suggest the claimed patient populations, and thus does not anticipate the pending claims.

To anticipate a claim, a reference must disclose each and every element of the claimed invention. *Verdergaal Bros. v. Union Oil Co. of Cal.*, 814 F.2d 628, 2 USPQ2d

1051 (Fed. Cir. 1987). Furthermore, "[t]o establish inherency, the extrinsic evidence 'must make clear that the missing descriptive matter is *necessarily* present in the thing described in the reference, and that it would be so recognized by persons of ordinary skill. Inherency, however, may not be established by probabilities or possibilities. The mere fact that a certain thing *may* result from a given set of circumstances is not sufficient.'" *In re Robertson*, 169 F.3d 743, 745 (Fed. Cir. 1999) (citations omitted) (emphasis added); *see also In re Rijckaert*, 9 F.3d 1531, 1534 (Fed. Cir. 1993) (CAFC reversed obviousness rejection because inherency was based on "optimal" conditions, and the means for achieving such "optimal" conditions were not explicitly or implicitly disclosed in prior art); M.P.E.P. § 2112, IV. Thus, the M.P.E.P. and the case law make clear that simply because a certain result or characteristic *may* occur in the prior art does not establish the inherency of that result or characteristic.

Doyle *et al.* is entitled "Surfactant as a Marker of Disease Severity in Critically Ill Patients with Respiratory Failure," and the abstract discloses the evaluation of plasma levels of surfactant protein A (SP-A) and surfactant protein B (SP-B) in such critically ill patients with respiratory failure. These critically ill patients in Doyle *et al.* suffered from either acute cardiogenic pulmonary oedema (APE) or acute respiratory distress syndrome (ARDS), and the SP-A and SP-B plasma levels for such critically ill patients were compared to those of "normal individuals (controls)" and "ventilated patients with no evidence of cardiorespiratory disease (OD)." According to Doyle *et al.*, the SP-B plasma levels for the critically ill patients suffering from APE or ARDS was significantly higher than the SP-B plasma levels for the individuals in the normal or OD groups. Thus, Doyle *et al.* disclose nothing more than the comparison of SP-B plasma levels between a highly afflicted, critically ill patient group and a group that was not so afflicted.

In contrast to the teachings of Doyle *et al.*, the method of the present invention, as currently recited in independent claim 1, includes a mammal that is "asymptomatic to lung damage or wherein the clinical diagnosis of lung damage in said mammal cannot otherwise be confirmed without the aid of one or more invasive procedures." Claims 52-56 and 63 ultimately depend from claim 51 and thus include this limitation as well. Similarly, the method of the present invention, as currently recited in independent claim 57, includes a mammal that is "asymptomatic to alveolo-capillary membrane damage or wherein the clinical diagnosis of alveolo-capillary membrane damage in said mammal cannot otherwise be confirmed without the aid of one or more invasive procedures." Claims 58-62 and 64 ultimately depend from claim 57 and thus include this limitation as well. That is, the methods of the pending claims do not cover just any mammal, but only those specifically recited mammals as articulated in the claims.

As would be understood by one of ordinary skill in the art, in determining an individual to be "asymptomatic" to lung damage or alveolo-capillary membrane damage, there is a higher degree of inquiry required than that undertaken in Doyle *et al.* in classifying an individual as "normal." The term "asymptomatic" denotes that a careful, observational assessment of the individual has been made by the clinician, typically including a physical examination of the individual accompanied by pertinent questions being asked by the clinician in the course of the clinician's evaluation of relevant criteria in assessing lung health.

In contrast to such asymptomatic individuals, the "normal" individuals as disclosed in Doyle *et al.* are characterized as simply not diagnosed with the diseases (*i.e.*, APE or ARDS) of the critically ill patients in Doyle *et al.* These "normal" individuals did not

have APE or ARDS, but they also were not necessarily "asymptomatic" to lung damage or alveolo-capillary membrane damage (*i.e.*, they could have been both "normal" as disclosed by Doyle *et al.*, yet not asymptomatic to lung damage or alveolo-capillary membrane damage as that term is understood by one of ordinary skill in the art).

For example, and for the convenience of the Examiner, Applicant has attached hereto an article by Martine Remy-Jardin *et al.*, *Morphologic Effects of Cigarette Smoking on Airways and Pulmonary Parenchyma in Healthy Adult Volunteers: CT Evaluation and Correlation with Pulmonary Function Tests*, Radiology, Volume 186(1):107-115 (1993) ("Remy-Jardin *et al.*"), which illustrates how an individual could be within the normal or OD groups of Doyle *et al.*, yet still not be within the scope of the patient populations of the pending claims. Remy-Jardin *et al.* discloses a study of 175 healthy adult volunteers, with no evidence of cardiorespiratory disease, separated into current smokers, ex-smokers and nonsmokers. *See* Remy-Jardin *et al.*, p. 107, col. 3 through p. 108, col. 1; and p. 112, col. 3. As can be seen in Table 2 of Remy-Jardin *et al.*, several of the healthy smokers were not asymptomatic to lung damage (*e.g.*, cough, wheezing, dyspnea present). As can be seen in Table 5 of Remy-Jardin *et al.*, several of the healthy smokers were diagnosed with emphysema via a high-resolution CT (HRCT) scan (*i.e.*, a non-invasive procedure). *See* Remy-Jardin *et al.*, Table 4; and p. 114, col. 2. Thus, the study of Remy-Jardin *et al.* could have included a healthy smoker with no evidence of cardiorespiratory disease, who was not asymptomatic to lung damage and who had lung damage (emphysema) which could be confirmed without the aid of an invasive procedure. Such an individual would be placeable within the normal or OD groups of Doyle *et al.*, yet not fall within the patient populations of the current claims.

Therefore, the normal and OD groups of Doyle *et al.* could theoretically consist of such individuals as the aforementioned healthy smoker as identified in Remy-Jardin *et al.* Thus, Doyle *et al.* does not disclose or suggest that a member of the normal group or OD group are necessarily "asymptomatic to" lung damage or alveolo-capillary membrane damage, or necessarily of a condition that the clinical diagnosis of lung damage or alveolo-capillary membrane damage in the mammal "cannot otherwise be confirmed without the aid of one or more invasive procedures." Doyle *et al.* therefore does not inherently anticipate the presently claimed invention.

That Doyle *et al.* does not anticipate the presently claimed subject matter is reinforced by the decision in *Eli Lilly v. Teva,* 2004 U.S. District LEXIS 14724. At issue in *Eli Lilly* was whether certain prior art clinical trials inherently anticipated a method of treatment claim, and the relevant facts are very similar to the present situation.

Lilly asserted claim 2 of its '998 patent, directed to a method of treating symptoms associated with pre-menstrual syndrome (PMS), including "disturbances of mood" by administering fluoxetine. *Id.* at *42. Fluoxetine was in the prior art to Lilly's patent as a well-known anti-depressant (the active in Prozac). *Id.* at *12-14. Teva, the accused generic infringer, argued that claim 2 of Lilly's '998 patent was inherently anticipated by a particular prior art clinical trial in which 112 adult women diagnosed with major depressive disorder were administered fluoxetine. *Id.* at *79-81. Teva asserted that treating major depressive disorder encompassed treating the later-claimed disturbances of mood associated with PMS. But in any event, Teva further argued, as supported by biostatistical analysis from an expert, that there was greater than 99.9999% certainty that one or more of the prior art cohort of 112 women was suffering from the mood disturbance of the claim. *Id.* at *80-81. This was based

on the documented prevalence rates of pre-menstrual depression among women with major depression disorder. *Id.*

The court ruled that the asserted prior art use of fluoxetine to treat depressive disorder did not inherently anticipate the claim to treating disturbances of mood. *Id.* at *81, *86-87. First, the court observed that the reason for administering fluoxetine in the prior art trial was to determine its effectiveness in treating major depressive disorder, and not PMS. *Id.* at *81. The same is analogously true here, where the sole purpose of measuring SP-B levels in the Doyle *et al.* patient populations was simply to see if those subjects having demonstrable, severe affliction exhibited higher SP-B levels than those that were not so afflicted, and not to determine if SP-B differences were sensitive enough to distinguish between individuals within the normal group, for example.

Second, the *Eli Lilly* court was not persuaded by the biostatistical evidence confirming the greater than 99.999% probability that one of the women in the prior art trial was indeed being treated for PMS-related mood disorders. The court, consistent with Federal Circuit precedent, concluded that the biostatistical evidence was based on probabilities, even "very strong" probabilities, but that a claim limitation is only inherent in the prior art "if it is necessarily present in the prior art, *not merely probably or possibly present*." *Id.* at *82 (emphasis in the original). The court reasoned, quoting *Continental Can Co. USA, Inc. v. Monsanto Co.*, 948 F. 2d 1264, 1269 (Fed. Cir. 1991), that "inherency... may not be established by probabilities or possibilities. The mere fact that a certain thing *may* result from a given set of circumstances is not sufficient." Id. (emphasis in the original).

The court observed that it could not be established with certainty that any one female in the prior art trial actually had PMS. Id. at *83. Likewise, in the present case, it

cannot be said that Doyle *et al.* certainly or necessarily discloses individuals asymptomatic to lung damage or having lung damage that could only be confirmed with invasive procedure, especially in view of the fact that one of skill in the art could readily contemplate an individual outside of the present claim (see example above in the Remy-Jardin *et al.* paper).

The *Eli Lilly* court also relied on the fact that PMS requires a careful diagnosis, and that none of the women in the prior art clinical trial were diagnosed with PMS because in that context, it was irrelevant to that trial. *Id.* at *20. Indeed, the court noted that the physicians conducting the trials did not interview the patients to obtain sufficient information to diagnose PMS. *Id.* at *22-23. Likewise here, there is no indication in Doyle *et al.* that the investigator-authors undertook the necessary steps to be able to draw the conclusion (and hence classify) a subject as asymptomatic, as it was irrelevant to the work's overall purpose of simply creating a comparison between the overtly afflicted and the not-overtly afflicted.

Thus, for at least the preceding reasons, it is respectfully submitted that the rejections under 35 U.S.C. § 102(b) have been overcome and should therefore be withdrawn.

IV. REJECTIONS UNDER 35 U.S.C. § 103(a)

Claims 51-64 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over Honda (Japanese Journal of Thoracic Diseases, 34 Suppl Abstract only, December 1996; reference A11 on PTOL-1449 of 6/6/00) in view of Doyle *et al.* and Abe *et al.* (Japanese Journal of Thoracic Diseases, 33(11):1219, Abstract only, November 1995; reference A10 on PTOL-1449 of 6/6/00). Applicant respectfully submits that these rejections should be withdrawn for at least the following reasons.

As described above in regard to the anticipation rejections, Doyle *et al.* does not disclose or suggest the claim recitation of "wherein the mammal is asymptomatic to lung damage or wherein the clinical diagnosis of lung damage in the mammal cannot otherwise be confirmed without the aid of one or more invasive procedures," as currently recited in claims 51-56 and 63. Likewise, Doyle *et al.* does not disclose or suggest the claim recitation of "wherein the mammal is asymptomatic to alveolo-capillary membrane damage or wherein the clinical diagnosis of alveolo-capillary membrane damage in the mammal cannot otherwise be confirmed without the aid of one or more invasive procedures," as currently recited in claims 57-62 and 64.

Neither Honda nor Abe *et al.* cure the shortcomings of Doyle *et al.* According to Honda, "the concentrations of SP-D and SP-A were measured in sera of patients with idiopathic interstitial pneumonia (IIP)," and then compared to "samples from healthy volunteers." Honda, lines 3-6. In Abe *et al.*, the serum SP-A levels in patients with idiopathic interstitial pneumonia, pulmonary alveolar proteinosis, and collagen disease with interstitial pneumonia were compared to those in healthy volunteers. *See* Abe *et al.*, lines 7-9. However, neither Honda nor Abe *et al.* disclose or suggest that the healthy volunteers are necessarily "asymptomatic to" lung damage or alveolo-capillary membrane damage, or that the clinical diagnosis of lung damage or alveolo-capillary membrane damage in the mammal "cannot otherwise be confirmed without the aid of one or more invasive procedures." In fact, as described above in regard to the anticipation rejections, Remy-Jardin *et al.* illustrates how a "healthy" smoker could be not asymptomatic to lung damage and have lung damage (emphysema) which could be confirmed without the aid of an invasive procedure. Once again, such an individual would be placeable within the healthy groups of Honda or Abe *et al.*, yet not fall within the patient populations of the current claims.

Thus, for at least the preceding reasons it is respectfully submitted that the rejections under 35 U.S.C. § 103(a) should be withdrawn.

V. CONCLUSION

In light of the foregoing, Applicant respectfully submits that all pending claims are in condition for allowance. Prompt reconsideration and allowance of the present application are therefore earnestly solicited.

Respectfully submitted,
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